Remarks

This is in response to the Official Action of December 8, 2004 and the Notice of Non-compliant Amendment of June 21, 2005. Claim 40 has been properly presented.

1. Section 112 rejections.

Claims 11-12, 14-17, 19-22, 24-27 and 29-30 stand rejected as lacking enablement under the first paragraph of 35 USC 112. Reconsideration is respectfully requested in light of the following comments on the *Wands* factors set forth in the Official Action.

With respect to "the nature of the invention", it is submitted that the invention is a "method of treatment". It is submitted that methods of treatment are well-settled subject matter, that the level of skill in the art of pharmaceutical sciences is high, and that, where an invention has been described as a method, such characterization has been considered a *Wands* factor favoring the grant of generic claims.

No mention in the official action is made of "the level of skill in the pertinent art". Level of skill must also be considered in evaluating enablement under the *Wands* line of cases. In this case the level of skill in the art is high and this factor weights in favor of the applicants.

"State of the art", another *Wands* factor, is consolidated with "the predictability or lack thereof in the art." Applicant respectfully objects. "State of the art" is characterized **separately** from "predictability of the art" under the *Wands* line of cases. In this case, the "state of the art" is highly developed, as reflected by (among other things) the numerous issued United States patents on the therapeutic use of antibodies and the broad commercial availability of techniques for "humanizing" antibodies for therapeutic purposes, all as discussed extensively in the instant specification.

Likewise, in addressing "predictability of the art", the official action relies upon the problems with rodent or unmodified antibodies. However, the claims are not so limited. Techniques for "humanizing" antibodies were widely available at the time the instant application was filed, are discussed extensively in the instant specification, and

persons skilled in the art would readily know how to "humanize" antibodies for use in the instant invention through routine product development procedures. Accordingly, this factor weights in favor of applicants.

With respect to "guidance in the specification", persons skilled in the art would be able to readily arrive at a pharmaceutical formulation and dosage for carrying out the present invention with the exercise of routine skill. As noted above, the specification provides extensive discussion of the humanization of antibodies, all of which can be carried out in accordance with routine skill.

While the official action is critical of the number of working examples, it is noted that the number of working examples alone, even in cases involving *ex vivo* therapeutic immunology, does not negate enablement. *See, e.g., In re Strahilevitz*, 212 USPQ 561 (CCPA 1982)(finding of lack of enablement for immunological method for removing a hapten from the blood of a mammal reversed).

While the claims presented are indeed generic, it is respectfully submitted that scope of the claims alone should not negate enablement where, as here, the remaining *Wands* factors weigh in favor of the grant of generic protection.

The present inventors made a noteworthy discovery: That the endothelial cell surface ATP synthase is active in ATP synthesis and is inhibited by angiostatin. *See, e.g.,* T Moser et al., *Proc. Natl. Acad. Sci. USA* **98**; 6656-6661 (June 5, 2001)(copy enclosed). From this noteworthy discovery and the teaching of the instant specification, the claimed invention can be readily applied through the exercise of routine skill. Accordingly, it is respectfully requested that the *Wands* factors be reevaluated in light of the comments above, and respectfully submitted that this rejection should be withdrawn.

2. Section 102 rejections.

Claims 48-52 stand rejected as anticipated under 35 USC 102(b) by **Dunn et al.** This rejection is respectfully traversed.

Dunn et al. uses an *Escherichia coli* ATPase which is only about sixty percent homologous to human ATPase. Given this dissimilarity, the skilled biochemist would

not expect an antibody that bound to *E. Coli* ATPase to also bind to a human ATPase.

Dunn et al. only determined the activity of antibody in interfering with the activity of enzyme in breaking down ATP, that is, as an ATPase, and not as an ATP synthase.

Dunn et al. only determined the activity of their antibody on membrane bound bacterial mitochondrial ATPase or plant chloroplast ATPase. they found that the enzyme was less active when membrane bound than the solubilized enzyme, apparently due to the different environment. Therefore Dunn et al. show that the activity of the antibody in affecting enzyme activity is highly dependent upon the environment in which the enzyme is found. The skilled biochemist would thus further doubt that the antibodies of Dunn et al. would have the properties of the claimed antibodies.

§ 2112 of the MPEP states that, when (as here) a recited feature of a claim is not expressly stated in the prior art, an official action must provide a rationale or show evidence tending to show inherency. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950–51 (Fed. Cir. 1999) states that:

> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probability or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'"

In this case, it is submitted that the references neither shows, nor gives assurance, that the characteristics found in the claims would be provided by the materials therein. Accordingly, it is respectfully submitted that this rejection should be withdrawn.

3. Section 103 rejections.

Claims 1-2, 4-6 and 48-52 stand rejected as obvious over US Patent No. 5786150 to **Hillman et al.** as evidenced by applicant's definitions on pages 11-12 of the specification. This rejection is respectfully traversed.

While the reference discusses the construction of antibodies to F_0 ATP synthase, the reference neither discloses nor suggests that antibodies be made to the region of ATP

synthas that is inhibited by angiostatin. Accordingly, it is respectfully submitted that this rejection should be withdrawn.

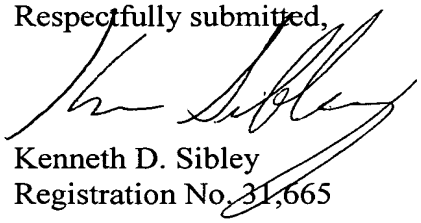
Claims 1-2 and 4-5 stand rejected as obvious under 35 USC 103(a) over US Patent No. 5837682 to **Folkman et al.** as evidence by applicant's definitions on pages 11-12 of the specification. This rejection is respectfully traversed. The reference suggests administering antibodies specific for angiostatin to humans to **reduce** angiogenic inhibition (column 5, lines 20-22). The presently elected invention is concerned with anti-angiogenic antibodies. Accordingly, it is respectfully submitted that this rejection should be withdrawn.

Claims 1 and 7 stand rejected as obvious over **Hillman et al.** or **Folkman et al.** in view of US Patent No. 6056973 to **Allen et al.** It is respectfully submitted that this rejection is obviated for the same reasons as set forth above, and respectfully submitted that this rejection should be withdrawn.

Claims 1 and 7 stand rejected as obvious over **Hillman et al.** or **Folkman et al.** in view of US Patent No. 6025353 to **Masferrer et al.** It is respectfully submitted that this rejection is obviated for the same reasons as set forth above, and respectfully submitted that this rejection should be withdrawn.

It is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,



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